

The role of saline infusion sonohysterography in the evaluation of infertility

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ABSTRACT

Aims: The study aimed to evaluate possible intrauterine pathologies that may not be visible in basal transvaginal ultrasonography in infertile patients using saline infusion sonohysterography.

Methods: Between January 2019 and January 2020, 110 patients who presented to the Ankara University Faculty of Medicine, Obstetrics and Gynecology Infertility Polyclinic were enrolled in the study. Saline infusion sonohysterography was performed on primary and secondary infertile patients who were not diagnosed with endometrial pathology via ultrasonography.

Results: Pathological findings were detected in 11 out of 110 patients (10.6%) during saline infusion sonohysterography, including polyps, myomas, and adhesions. These patients were referred to hysteroscopy by their practitioner. After the procedure, pathological findings were detected in 54.5% of cases by hysteroscopy. According to these data, the sensitivity of saline infusion sonohysterography in detecting intracavitary pathologies was 60%, specificity was 80.7%, positive predictive value was 54.5%, negative predictive value was 84%, and reliability was 75%.

Conclusion: Saline infusion sonohysterography can detect endometrial pathologies not identified by TV USG, suggesting its cost-effective addition to routine evaluations for infertile patients and potential endometrial pathologies.

Keywords: Saline infusion sonohysterography, infertility, endometrium, ultrasonography

INTRODUCTION

Infertility is generally defined as the inability to achieve pregnancy after one year of regular, unprotected sexual intercourse.¹ The global prevalence of infertility is between 8-12%.² This means that approximately 15% of couples are affected by infertility. However, the prevalence of infertility may vary across countries and age groups.³

Currently, the tests performed at the first consultation of infertile couples include semen analysis, evaluation for infectious diseases and cervical evaluation, ovarian reserve tests and evaluation of ovulation, and assessment of uterine cavity and tubal patency.⁴ Among these tests, transvaginal ultrasound (TV USG) and hysterosalpingography (HSG) are commonly used for the evaluation of the endometrial cavity.⁵ Hysteroscopy, which was frequently used in the past for initial evaluation, is no longer used for this purpose as it is an invasive procedure that requires anesthesia and cannot provide information about the myometrium and adnexa.⁶ Saline infusion sonohysterography (SIS)

is a method that is cheap, well-tolerated, and applied without exposure to radiation for the evaluation of the endometrial cavity.⁷ In addition, SIS has been shown to have no significant adverse effects and is a cost-effective method.⁸

Previously, other methods such as TV USG, HSG, and office hysteroscopy have been compared for the evaluation of the endometrial cavity in infertile patients.⁹⁻¹¹ In this study, the aim was to evaluate potential intrauterine pathologies that were not detected in basal TV USG with SIS in infertile patients.

METHODS

The study was carried out with the permission of Ankara University Clinical Researches Ethics Committee (Date: 26.11.2018 Decision No: 19-1301-18). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

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Study Design and Data Collection

Between January 2019 and January 2020, patients who applied to the Infertility Clinic of the Department of Obstetrics and Gynecology, Ankara University Faculty of Medicine, were evaluated. Among the 1208 patients who met the criteria and accepted the procedure, those who were between the ages of 20-35 and had normal TV USG findings were included in the study as primary or secondary infertility patients. Patients with a history of systemic endocrinological disease or previous uterine surgery were excluded from the study. Detailed medical history was obtained from each patient, and routine investigations including TV USG for endometrial thickness and adnexal pathology, hormonal profile on day 3, HSG, and semen analysis for male infertility evaluation were performed. Eligible patients were provided with detailed information about the study. As can be seen in the details in **Figure**, 110 patients who agreed to participate and signed the informed consent form were included in the study.

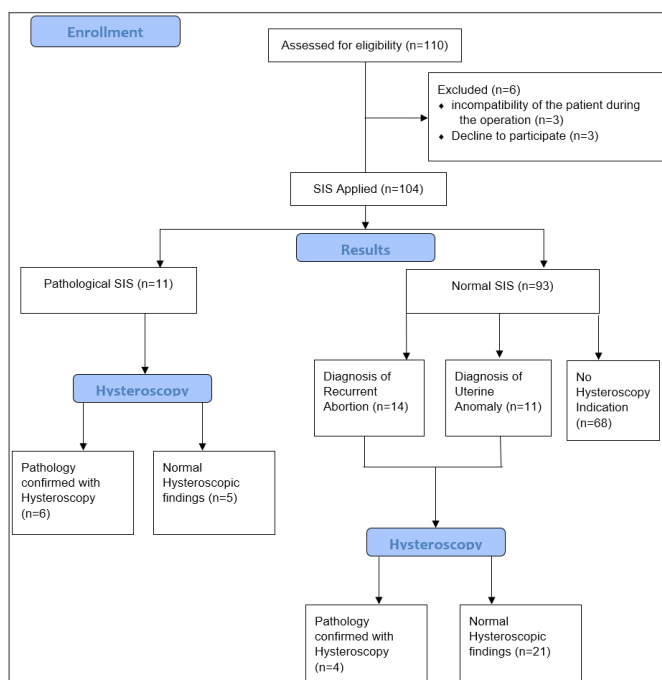


Figure. CONSORT 2010 Flow diagram

SIS Procedure

Patients included in the study were subjected to SIS on the 5th-6th day of their menstrual cycle. All procedures were performed by the same operator. The cervix was visualized with a speculum in the lithotomy position on the gynecological table. Povidone iodine solution was applied to the cervix, and then it was grasped with a tenaculum at the upper end. We utilize the tenaculum to facilitate the accurate insertion of the catheter into the uterine cavity, as well as to prevent any potential oversight of pathologies resulting from uterine malpositioning and to ensure standardization among patients. The cervical

ostium was reached with a HSG catheter, and the balloon was inflated. The speculum was removed, and the TV ultrasound probe was inserted into the vagina. Approximately 5-10 cc of saline was injected through the catheter, and the uterine cavity was observed.

Statistical Analysis

Software program SPSS 28.0.1 (IBM Corp., Armonk, NY, USA) was used to analyze the data. The distribution of the parameters was evaluated using the Kolmogorov-Smirnov test. The mean and standard deviation were used to describe the data. The G Power 3.1.9.7 software was used to determine the sample size based on the referenced article. According to these calculations, it was concluded that at least 98 patients should be included in the study.

RESULTS

The average age of patients included in the study was calculated as 28.8 ± 5.8 years. Their mean BMI was calculated as 25.75 ± 4.7 kg/m². The TV USG showed that the ovaries of 19 patients had a multifollicular appearance. The AMH value of 12 patients was below 1 ng/ml (**Table 1**).

Table 1. Demographic Results	
Demography	Mean±SD
Age (year)	28.8±5.8
BMI (kg/m ²)	25.75±4.7
Infertility period (year)	5.3±4.4
Infertility Status	
N (%)	
Primary	92 (88.5%)
Secondary	12 (11.5%)
Multifollicular ovarian morphology	19 (18.2%)
AMH <1 ng/ml	12 (11.5%)

The average infertility duration of patients who underwent SIS was calculated as 5.37 ± 4.4 years. Twelve patients had secondary infertility (11.5%), 8 had male infertility (7.6%), and the remaining patients were evaluated as having infertility with an unknown cause.

Intracavitary pathology was not detected in the TV USG and HSG evaluations of these patients. Patients who were found to have septum or t-shaped uterus appearance in HSG were evaluated as having uterine shape anomaly and were not considered as endometrial pathology, and included in the study

Three patients who met the criteria were not treated during the procedure due to their incompatibility. The procedure was postponed in 7 patients who had findings compatible with active pelvic infection. Cultures were taken from the patients, appropriate treatments were given, and new appointments were made for the procedure. The procedure was performed on 3 of these 7 patients. Pathological filling defects were detected

in 11 of the 104 patients (10.6%) who underwent SIS. Hysteroscopy was performed on these patients. After hysteroscopy, pathologies such as polyps, myomas, and adhesions were detected in 6 patients (54.5%).

Hysteroscopy was performed on 14 of the 93 patients whose SIS result was normal due to recurrent pregnancy loss diagnosis and on 11 patients due to a diagnosis of uterine shape anomaly. Endometrial polyps were detected in 4 cases and these polyps were 2-5 mm in diameter and located near the tubal ostium. The endometrial cavity was evaluated as normal in 21 cases. No complications were observed in the patients after the procedure.

According to our calculations with these data, the sensitivity of SIS in detecting intracavitary pathologies was calculated as 60%, specificity as 80%, positive predictive value as 54.5%, and negative predictive value as 84% (**Table 2**).

Table 2. Detection status of intracavitary pathologies of SIS			
	Hysteroscopy positive	Hysteroscopy negative	
SIS positive	6	5	54.5% (PPV)
SIS negative	4	21	84% (NPV)

DISCUSSION

Fertility problems are a health issue that affects both individuals and society, with biological, social, cultural, and psychological dimensions. In a study, it was found that about 10-15% of couples who want to conceive are unable to do so and seek medical attention.¹² Among infertile couples who begin treatment, abnormal uterine cavity findings are observed in approximately 34-62%.^{9,13}

The first option to evaluate the uterine cavity is usually TV USG. This is a non-invasive and relatively simple procedure where a specially designed ultrasound probe is inserted into the vagina to visualize the uterus, endometrium (lining of the uterus), and ovaries.¹⁴ TV USG can help identify structural abnormalities or pathology such as uterine fibroids, polyps, adhesions, or abnormalities of the endometrial lining that may affect fertility or menstrual function. If necessary, further tests such as SIS, HSG or hysteroscopy may be performed to provide more detailed information.¹²

Direct visualization and treatment of the uterine cavity is an advantage of the gold standard method hysteroscopy.¹⁵ However, hysteroscopy is an expensive method that requires operating room conditions and anesthesia.¹⁶ The inSIGHT study, a multicenter randomized study evaluating the routine use of hysteroscopy as a diagnostic method, showed that hysteroscopy did not change the live birth rate and was not recommended to be performed before the first IVF treatment in asymptomatic patients.¹⁷

In a study by Yu et al.¹⁸ 215 women underwent hysteroscopy before their first IVF cycle, while 284 women only received TV USG. Both groups were similar in terms of demographic and clinical characteristics. There were no significant differences in cycle pregnancy rate (CPR) (43% versus 44%), miscarriage rate (15.2% versus 16%), and live birth rate (LBR) (34% versus 35.6%) between the two groups. It was concluded that hysteroscopy performed before IVF treatment did not change the implantation or live birth rates.

Another study involved 421 patients between 24-40 years old who had undergone multiple failed IVF cycles with good quality embryo transfers. They were randomly divided into two groups: Group I (211 patients) did not undergo an office hysteroscopy evaluation before IVF treatment, while Group II (210 patients) did. Group II was further divided into two subgroups: IIa (154 patients) with normal hysteroscopic findings and IIb (56 patients) with abnormal findings. The study found no significant differences in terms of first-trimester abortions across all groups.¹⁹

According to a study by Aslam et al.²⁰ SIS had higher sensitivity and specificity compared to TV USG. Specifically, SIS had 92.9% sensitivity and 89.7% specificity, whereas TV USG had 71.4% sensitivity and 67.7% specificity. Additionally, there was higher agreement between SIS and hysteroscopy compared to TV USG. SIS demonstrated better diagnostic performance for endometrial hyperplasia, polyps, and submucous myoma compared to TV USG, with SIS showing 100% sensitivity and specificity for submucous myoma compared to 61.55% and 97.7%, respectively, for TV USG. In our study, SIS was able to detect 60% of the pathologies that could not be detected by TV USG. We believe that the reason for the sensitivity remaining at around 60% in these patients is due to the small size of the polyps in these cases, which are located near the tubal ostium.

In another study conducted by Brown et al.⁹ HSG, SIS, and office hysteroscopy were compared with hysteroscopy. Patients were evaluated with each of the three radiological methods on separate outpatient visits. If pathology was detected, the patient was admitted for operative hysteroscopy under anesthesia. Of the 46 patients in the study, pathology was detected in at least one method in 27 patients, who were then referred for hysteroscopy. It was noted that only 33% of the identified pathologies were detected by all three radiological methods. Similarly, 60% of the pathologies observed in hysteroscopy were correctly classified in HSG, 72% in office hysteroscopy, and 52% in SIS. Additionally, when the 25 patients examined with SIS were compared to hysteroscopy, a correct diagnosis was made in 13 patients

(54%). Similarly, in our study, out of the 11 patients where SIS detected pathology, a correct diagnosis was made in 6 (54.54%), which is consistent with the literature.

Obajimi et al.²¹ published a retrospective analysis of data from a clinic that routinely performed SIS before IVF treatment. Of the 760 patients reviewed, pathology was detected in 349. The sensitivity of SIS was calculated as 96% compared to hysteroscopy performed later in these patients. In our study, we calculated a sensitivity of 60%. The difference in rates may be due to the higher number of patients in the study by Obajimi et al.²¹ additionally, the small size and proximity to the tubal ostium of polyps that we could not detect with SIS may also contribute to this difference.

Radwan et al.²² also conducted a study to evaluate the role of SIS in the assessment of endometrial polyps in patients diagnosed with infertility. The study compared SIS and hysteroscopy in 241 infertile patients, and endometrial polyp diagnosis was confirmed by both hysteroscopy and SIS in 72 patients. Seven patients were suspected to have polyps on SIS but were not seen on hysteroscopy, and two patients had no pathology on SIS but were found to have polyps on hysteroscopy. The study did not provide information on whether TV USG findings showed pathology in patients. However, in our study, we included only patients with normal TV USG findings. Although hysteroscopy was performed in every patient in Radwan et al.'s study, recent studies have shown that performing hysteroscopy does not provide additional benefits. Furthermore, it was found that hysteroscopy to identify 72 polyps in 241 patients would not be cost-effective, and SIS was deemed sufficient. Radwan et al.²² also noted that the polyps that were not detected on SIS were located near the tubal ostium and had dimensions of 2×3 mm. It was concluded that these undetected polyps could not be seen on SIS due to their small size and location near the tubal ostium. Similarly, in our study, the polyps that were not visible on SIS had small dimensions and were located near the tubal ostium.

Despite the advanced technology of TV USG, endometrial pathologies may still go undetected. In this study, we aimed to evaluate potential endometrial pathologies in cases where no pathology was detected by TV USG, using SIS, which allows for more advanced evaluation of the endometrial cavity.

Our study included 104 patients, and SIS detected additional endometrial pathology in 10.6% of cases where no pathology was detected by TV USG. Therefore, considering SIS as a patient-friendly examination, we believe that it should be included in routine infertility evaluations.

Our study had some limitations; although our sample size was adequate, we were unable to compare the cost-effectiveness and patient comfort of SIS to other testing techniques in a single sentence, necessitating further research to potentially establish SIS as a routine procedure. Moreover, we did not perform hysteroscopy on all patients, as it was not recommended as a routine procedure in previous multicenter randomized controlled prospective studies. Consequently, our assessment of the sensitivity and specificity of SIS may have been limited. The inclusion of hysteroscopy could have provided a more comprehensive evaluation of the diagnostic accuracy of SIS. In order to further assess SIS, we could have evaluated patients' pain experiences; however, the use of the tenaculum, which was employed to assess diagnostic boundaries and standardize patients in our study, hindered the evaluation of the pain scale. In future studies, the advantages of performing the SIS procedure without using a tenaculum in terms of patient comfort can be assessed.

CONCLUSION

We aimed to demonstrate that endometrial pathologies could be detected by SIS even when not identified by TV USG. Based on these results, we believe that SIS is a cost-effective application and should be included in the routine evaluation of not only infertile patients but also all potential endometrial pathologies, in addition to TV USG.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara University Non-invasive Clinical Researches Ethics Committee (Date: 26.11.2018, Decision No: 19-1301-18).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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